REMARKS

Claim 1 was pending before the Office. Claim 1 is hereby amended. New claims 2-8 are added. No claims are cancelled. Accordingly, claims 1-8 shall be pending upon entry of this amendment.

The amendments made herein have been made solely to claim more fully the invention and/or to expedite prosecution of the present application and should in no way be construed as an acquiescence to any of the Examiner's rejections in the Office Action issued in the present application. Applicants reserve the right to pursue the subject matter of the claims as originally filed or similar claims in one or more subsequent applications.

Support for the amendments can be found throughout the originally-filed application, including the specification, drawings, examples and claims. No new matter has been added by this amendment.

Applicants believe the amendments overcome the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under Section 112, second paragraph.

Claims Rejections – 35 USC § 112

The Office Action rejects claim 1 as allegedly being indefinite for the reason that it does not set forth any method steps, and that, as such, the claimed method is unclear. While Applicants do not necessarily agree with the Examiner's rejection, the claims have been amended to clarify the claimed invention. Thus, claim 1 was amended to specify a method to improve permeation of a pharmaceutically active substance across a cell barrier comprising co-

administering the pharmaceutically active substance with a compound of formula I together with compound 1 or compound 2 of claim 1.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under Section 112, first paragraph.

Claims Rejections – 35 USC § 101

The Office Action rejects claim 1 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter because claim 1 is drawn to a use without setting forth any steps involved in the process, and thus, not a process under 35 U.S.C. § 101. While Applicants do not necessarily agree with the Examiner's rejection, the claims have been amended to clarify the claimed invention. Accordingly, claim 1 now specifies a method to improve permeation of a pharmaceutically active substance across a cell barrier comprising co-administering the pharmaceutically active substance with a compound of formula (I) together with compound 1 or compound 2 of claim 1.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under Section 101.

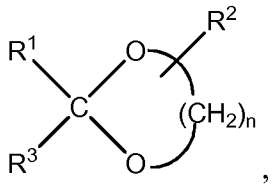
Claim Rejections – 35 U.S.C. 102

The Office Action rejects claim 1 under 35 U.S.C. § 102(b) as allegedly being anticipated by Samour et al. (U.S. Patent No. 4,861,764) ("SAMOUR"). The Office Action also rejects claim 1 under 35 U.S.C. § 102(b) as allegedly being anticipated by Fuhrman Jr. et al., "Effect of novel penetration enhancers on the transdermal deliver of hydrocortisone: an in vitro species comparison," Journal of Controlled Release (1997) 45: 199-206 ("FUHRMAN"). Claim 1 further stands rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Hui et al.,

"Enhanced econazole penetration into human nail by 2-n-nonyl-1,3-dioxolane," Journal of Pharmaceutical Sciences (2002) 92; 142-148 ("HUI"). Applicants disagree with the rejections and respectfully traverse as follows.

As a first matter, the Examiner is respectfully pointed to the M.P.E.P § 2131 which states that "[a] claim is anticipated ***only if each and every element*** as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (emphasis added). It will be shown below that SAMOUR, FUHRMAN and HUI, either standing alone or in combination, do not expressly or inherently teach each and every element of the claimed invention, and thus, do not anticipate the present claims.

Turning to the present invention, claim 1 is directed to a method to improve permeation of a pharmaceutically active substance across a cell barrier comprising co-administering the pharmaceutically active substance with at least two different compounds of the formula (I):



,

in which

R^1 represents an alkyl, alkenyl or alkynyl radical which has 2 to 30 carbon atoms and which is optionally substituted by one or more halogen atoms, wherein one or more suitable nonadjacent carbon chain members can optionally be replaced by oxygen atoms,

R^2 represents hydrogen, hydroxyl, $-NH_2$, $-NR^4R^5$, $-N^+(R^4R^5R^6)$, $-PR^7R^8$, $-O-P(R^7R^8)$, $-P(O)R^7R^8$, $-P^+(R^7R^8R^9)$ or a C_{1-5}-alkyl radical which is optionally substituted by

hydroxyl, C_{1-4}-alkoxy, $-NH_2$, mono- or di-C_{1-4}-alkylamino or a 5- to 7-membered heterocycle having up to three hetero atoms selected from among O, N and S,

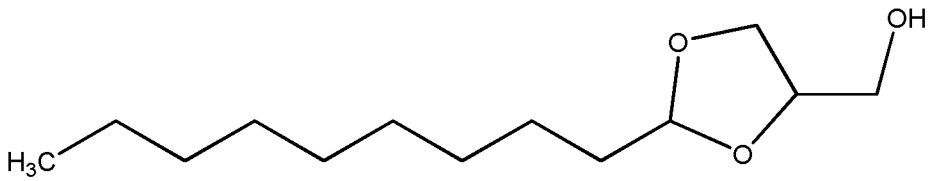
R^3 represents hydrogen or can have the meanings stated above for R^1,

R^4, R^5 and R^6 independently of one another represent hydrogen or C_{1-5}-alkyl or two of the radicals together with the nitrogen atom to which they are bonded from a 5- to 7-membered heterocycle which can optionally additionally comprise one or two further heteroatoms selected from among O, N and S, R^7, R^8 and R^9 independently of one another represent C_{1-5}-alkyl, C_{1-5}-alkoxy or C_{6-12}-aryl

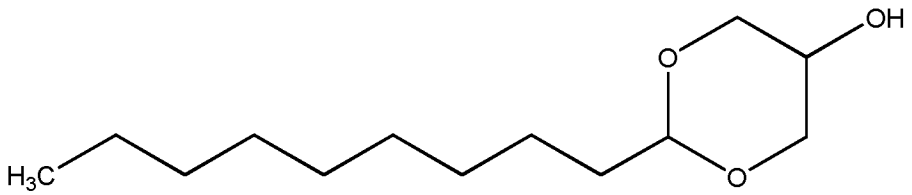
or

two of the radicals together with the phosphorus atom to which they are bonded form a 5-7-membered heterocycle which can optionally additionally comprise one or two further heteroatoms selected from among O, N and S,

n denotes 2, 3 or 4, wherein at least one of the compounds is



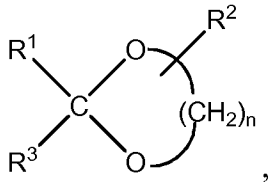
or



.

In claim 2, the application is further directed to a method to improve permeation of a pharmaceutically active substance across a cell barrier comprising co-administering the

pharmaceutically active substance with at least two different compounds of the formula (I):



,

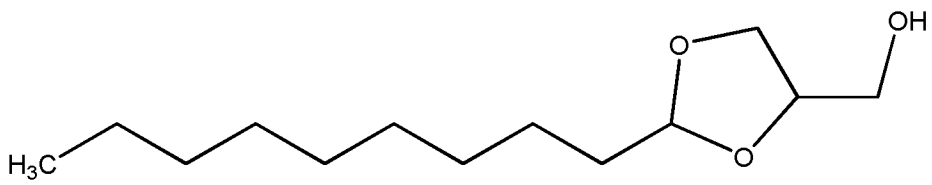
in which

R^1 represents an alkyl which has 2 to 20 carbon atoms and which is optionally substituted by one or more fluorine or chlorine atoms, wherein one or more suitable nonadjacent carbon chain members can be replaced by an oxygen atom,

R^2 represents hydroxyl or C_{1-3}-alkyl optionally substituted by hydroxyl or C_{1-5}-alkoxy,

R^3 represents hydrogen,

n denotes 2 or 3, wherein at least one of the compounds is



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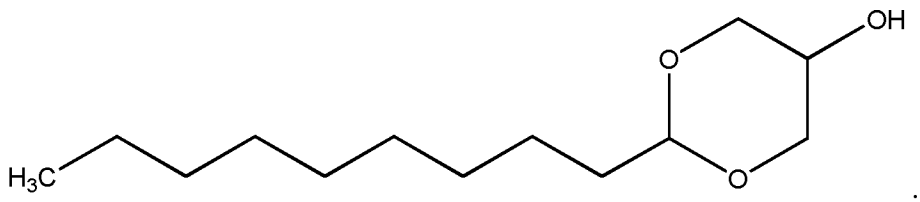

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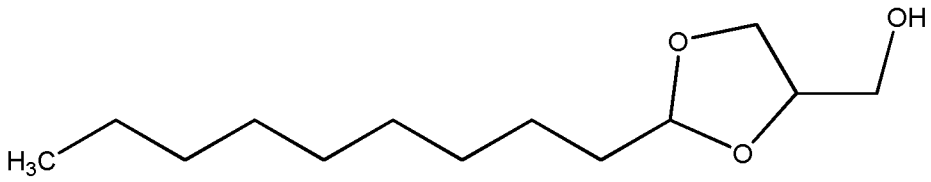
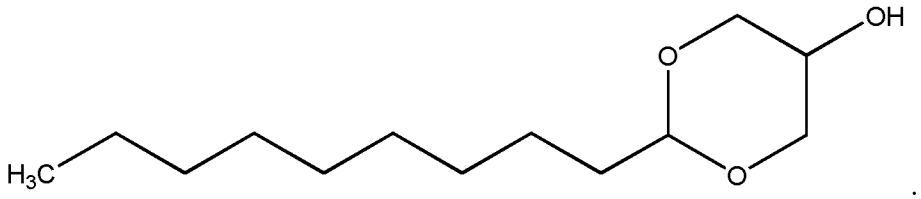
Further still, claim 3 specifies a method to improve permeation of a pharmaceutically active substance across a cell barrier comprising co-administering the pharmaceutically active substance with compound 1:

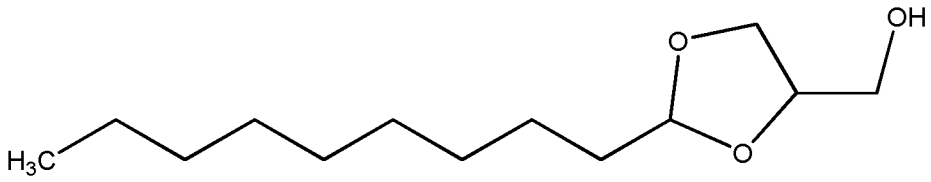


and compound 2:

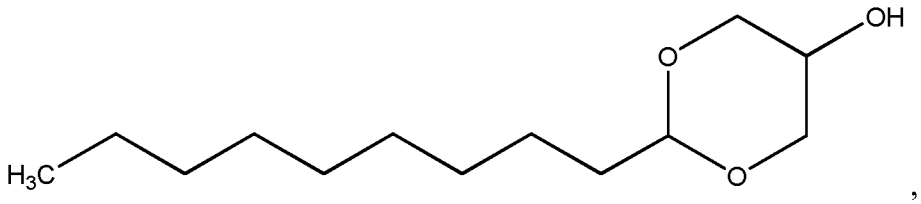


.

The invention is also directed to, as specified in claim 7, a composition to improve permeation of a pharmaceutically active substance across a cell barrier comprising compound 1:



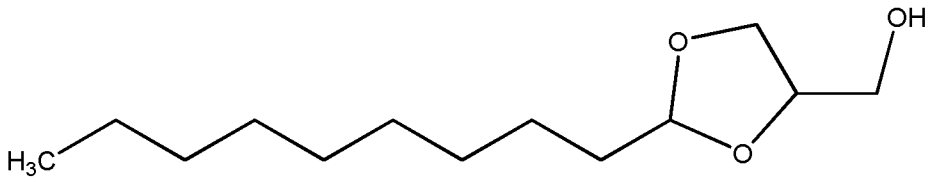
and compound 2:



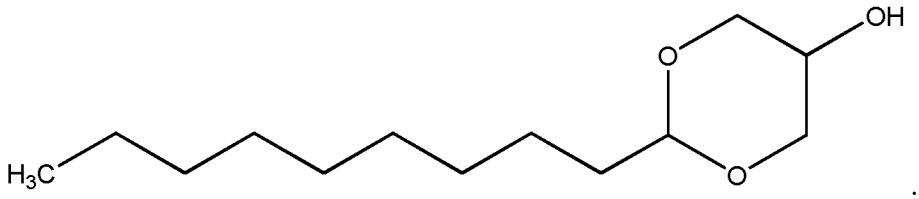
,

and a pharmaceutically acceptable carrier, wherein compound 1 and compound 2 are present in a ratio of about 9:1.

As can be seen, each of the claims of the present invention require the presence of at least compound 1:

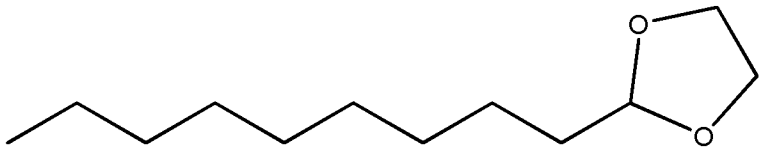


or compound 2:

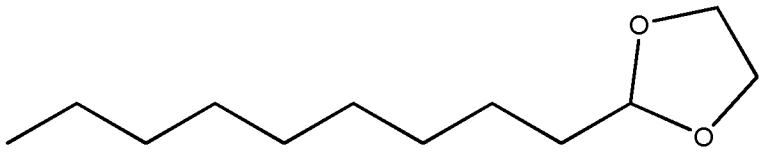


.

Turning to the references, SAMOUR relates to 1,3-dioxacyclohexanes and 1,3-dioxacyclopentanes as penetration enhancers. FUHRMAN reports on a study of penetration enhancers, including 2-(1-nonyl)-1,3-dioxolane,

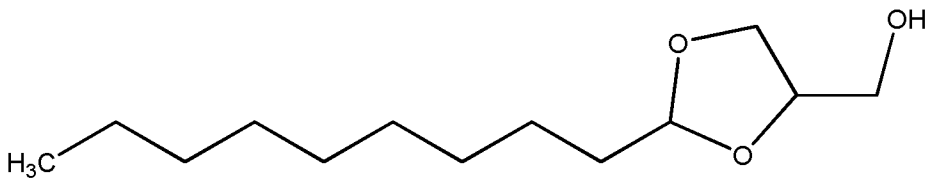


2-(1-nonyl)-1,3-dioxolane , used to facilitate the percutaneous penetration of certain drugs through the skin. HUI relates to a study to enhance the penetration of econazole through human nail by 2-n-nonyl-1,3-dioxolane,

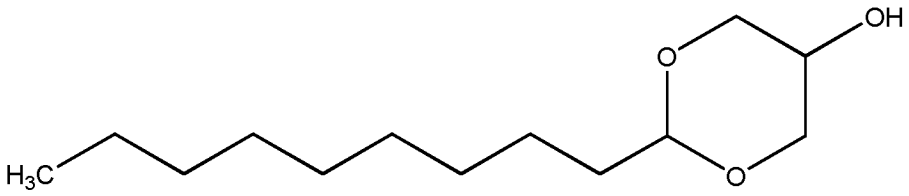


2-n-nonyl-1,3-dioxolane . Unlike all of the claims of the present invention, however, SAMOUR, FUHRMAN and HUI each fail to teach or suggest the particular combination of compounds claimed in the instant application. In particular, unlike

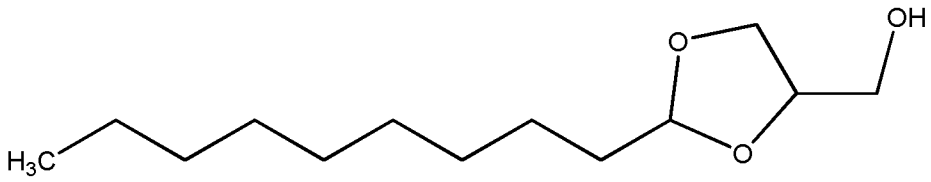
claims 1 and 2, SAMOUR, FUHRMAN and HUI do not teach or fairly suggest a method which involves administering a composition which includes a compound of formula I co-administered with either compound 1



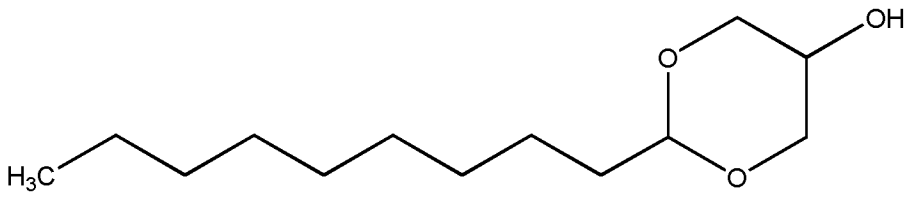
or compound 2:



. Moreover, SAMOUR, FUHRMAN and HUI do not teach or suggest, unlike in claim 3, a method for improving the permeation of a pharmaceutically active substance across a cell barrier comprising co-administering the pharmaceutically active substance with compound 1:



and compound 2:



or, unlike claim 8, a composition comprising compound 1 and 2.

Because SAMOUR, FUHRMAN and HUI, either alone or in any combination, do not

teach or suggest each and every element of all of the claims of the instant application, the rejections under 35 U.S.C. § 102(b) should be reconsidered and withdrawn.

CONCLUSION

In view of the remarks herein, Applicants respectfully request reconsideration and withdrawal of all of the rejections as Applicants believe the application to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

Dated: July 16, 2008

Respectfully submitted,

By: /Gabriel J. McCool/

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